CASE REPORTS

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Toxicity by Interaction of Tricyclic Antidepressant and Monoamine Oxidase Inhibitor

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A PATIENT RECENTLY SEEN at the Sacramento Medical Center had a hyperpyretic crisis and then shock caused by the incompatible interaction of tranylcypromine (Parnate®) and desipramine (Norpramin®). Monoamine oxidase inhibitors are known to interact with sympathomimetic amines to produce hypertensive crises, to potentiate the effects of various central nervous system depressants (for example, narcotics, alcohol, barbiturates) and to produce various acute crises when given with central nervous system stimulants.[1,2,3] The problem of avoiding these deleterious drug interactions is magnified when patients do not remember what medications they are taking, nor for how long they have taken them, as in the following case.

Report of a Case

A 60-year-old white woman was admitted to the psychiatric ward of the Sacramento Medical Center (SMC) in August, 1970, for evaluation of involutional depression. She was given amitriptyline (Elavil®) and discharged to the care of her private physician. Subsequent medications included thyroid extract, 1 grain daily, hydrochlorothiazide, 50 mg daily, ethachlorvynol (Placidyl®) 750 mg for sleep, and tranylcypromine (Parnate) 10 mg twice daily, starting in early November, 1971. On November 19, 1971, she came to SMC complaining of weakness and fatigue. She was thought to have a depressive neurosis since she was acutely upset and unable to remember her medications. She was given desipramine (Norpramin) 50 mg tablets to be taken thrice daily.

On November 26, 1971, her son brought her to SMC because of fever. She was agitated and her behavior bizarre but on examination no other abnormality was noted. The white blood cell count was 7,900 per cu mm with 68 percent neutrophils; the hemoglobin, hematocrit, blood glucose, blood urea nitrogen, serum sodium, potassium, chloride, and bicarbonate values were all within normal limits. Since none of the previous history of illnesses or medications was known, the cause of the fever was not clear. Therefore, the patient was placed in the observation unit for the night. At 4 a.m. her rectal temperature was 104° F, she had pronounced hyperreflexia and flexor plantar reflexes, and she was disoriented as to time, person, and place, with increasing confusion and agitation. She was transferred to an in-patient ward. The rectal temperature rose to 107.6° F, and cooling was instituted immediately. Further examination demonstrated pronounced bilateral nystagmus, mydriasis, opisthotonus, bilateral Babinski signs, a gross tremor with muscle twitching, and obtundation. The cerebral spinal fluid was clear and the chemical values within normal limits. An electrocardiogram showed no abnormality but sinus tachycardia. Nasogastric tube aspirate was initially hematest-positive but cleared, and no capsules were returned. Arterial blood gases were pCO_2 42 mm of mercury, pH 7.38 and pO_2 59 mm of mercury.

A working diagnosis of tricyclic overdosage

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was made. As the temperature fell toward normal the blood pressure dropped from 120/80 to 70/30 mm of mercury. Despite the administration of five liters of fluid, shock persisted, and norepinephrine drip was cautiously started.

The patient was transferred to intensive care where her blood pressure stabilized and she gradually became responsive. She had no seizure activity during her course. Digoxin 0.25 mg and furosemide (Lasix®) 40 mg were given intravenously to support cardiac function and augment urine output. It was soon learned that she had taken 30 tablets of tranylcypromine over the preceding three weeks in addition to five desipramine tablets the past six days. A gas chromatography screening, including salicylates, was negative; two blood cultures were negative and tests of thyroid function were all normal. Creatinine phosphokinase, lactic dehydrogenase, and serum glutamic oxaloacetic transaminase were all elevated but rapidly fell toward normal.

The clinical syndrome could be explained entirely by the interaction between the tranylcypromine and desipramine. The patient improved rapidly except for a few involuntary muscle twitches that also disappeared. Psychiatric consultants believed no brain damage had been done by hyperpyrexia and agreed to observe her as an outpatient upon discharge one week later.

Discussion

The combination of a tricyclic and a monoamine oxidase inhibitor may produce symptoms of dizziness, headache, nausea, vomiting, hyperexcitation, muscle spasm, convulsions, decerebrate rigidity, severe hyperpyrexia, bizarre behavior, and hypo- or hypertension with pronounced individual variation in sensitivity to the combination.[1,3] The severity of the situation must be stressed, since death is not a rare eventuality. Monoamine oxidase inhibitors are thought to produce irreversible inhibition of the enzyme; hence, it is necessary to allow two weeks after cessation of the drug for monoamine oxidase to reaccumulate before administering a drug with a potential interaction.[2] The mechanism of action of Norpramin® (desipramine hydrochloride), a rapidly-acting tricyclic, and of its interaction with a monoamine oxidase inhibitor is unknown. The most common adverse effect seen with the monoamine oxidase inhibitors is the hypertensive crisis in which an indirectly-acting amine (for example, tyramine in certain cheeses) is ingested, this causing acute elevation of blood pressure due to an exaggerated norepinephrine release.[2]

In 1964 tranylcypromine sulfate (Parnate) was temporarily removed from the market because of associated headache, increased blood pressure, and cerebrovascular accidents. An estimated three and a half million persons had taken the drug. In recent years it has been replaced by the tricyclic antidepressants. Monoamine oxidase inhibitors continue in use. For example, phenelzine sulfate (Nardil®) recently was used to suppress rapid eye movement sleep in treating intractable narcolepsy.[4]

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Refer to: Rahbari H: Congenital absence of pectoral muscles. Calif Med 117:66-68, Dec 1972

Congenital Absence of Pectoral Muscles

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THE ABSENCE OF pectoralis major muscle is probably the most innocuous cause of unilateral hyper-radiolucent lung (Table 1). A recent case of unilateral hyperradiolucent lung proved to be due to this congenital absence.

Report of a Case

The patient was a short, stocky, 30-year-old Caucasian man who was in hospital for acute psychiatric treatment. On a routine chest roentgenogram the radiologist noted left unilateral

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